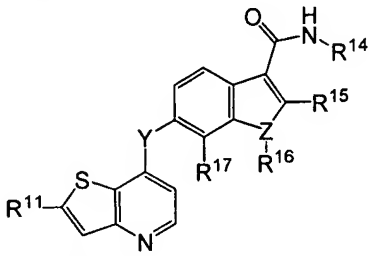
REMARKS

The invention as defined by the claims is directed towards N-substituted 3-carboxamido thienopyridine compounds of formula:



wherein Y, Z, R^{11}, R^{14}, R^{15}, R^{16} and R^{17} are as described, or pharmaceutically acceptable salts or solvates thereof.

Claims 52-79, 102 and 103 are pending in this application. Claims 80-101 are canceled herein without prejudice or disclaimer. Applicant retains the right to file divisional applications towards any canceled subject matter. A Request for Continued Examination (RCE) under 37 C.F.R. 1.114 of this application is enclosed with this response.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The Office Action has confirmed the rejection of claims 80-101 under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement.

As amended herein, claims 80-101 are canceled, which renders the rejection of these claims moot.

Rejection of Claims 80-101 Under 35 U.S.C. § 112, Second Paragraph

The Office Action has confirmed the rejection of claims 80-101 under 35 U.S.C. § 112, second paragraph as allegedly being indefinite.

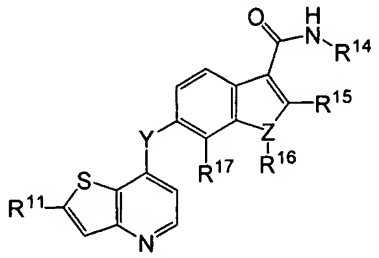
As amended herein, claims 80-101 are canceled, which renders the rejection of these claims moot.

Rejection of Claims Under 35 U.S.C. § 103(a) Over Munchhof et al. (WO 99/24440)

The Office Action has confirmed the rejection of claims 52-71 and 80-103 under 35 U.S.C. § 103(a) as allegedly being obvious over Munchhof et al. (WO 99/24440). Applicant respectfully disagrees.

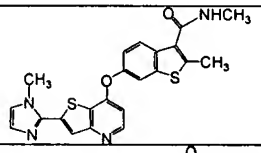
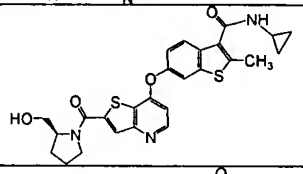
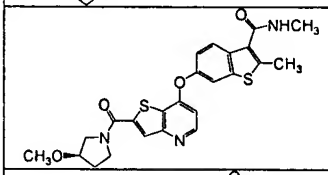
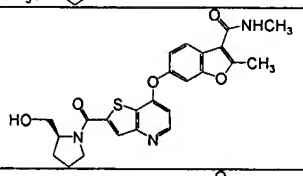
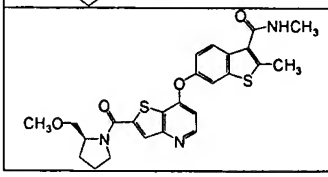
As amended herein, claims 80-101 are canceled, which renders the rejection of these claims moot.

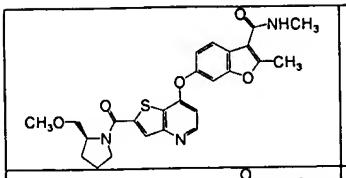
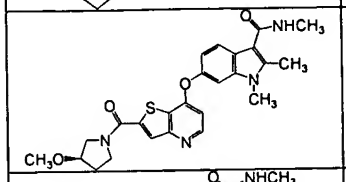
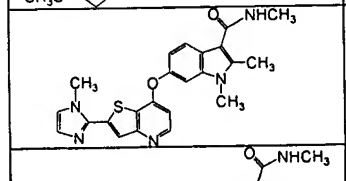
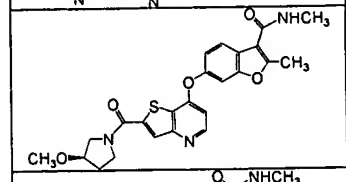
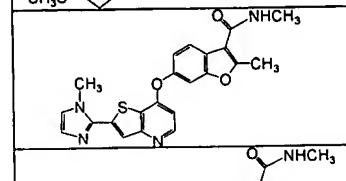
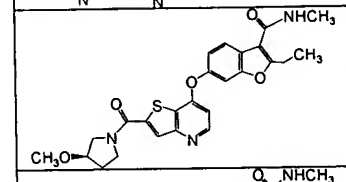
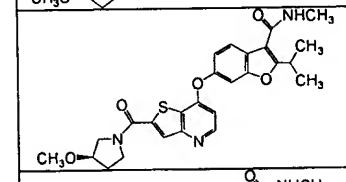
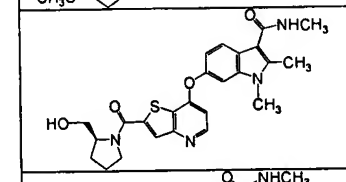
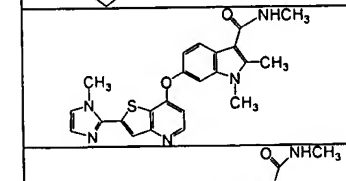
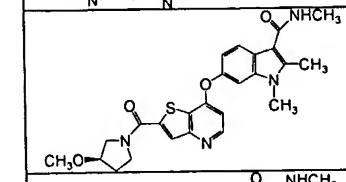
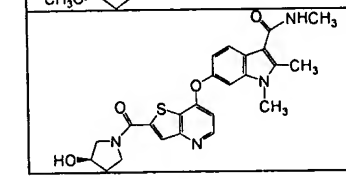
The invention as defined by the claims distinguishes over Munchoff by claiming N-substituted 3-carboxamido-6-heterocyclic thienopyridine compounds of formula:



wherein Y, Z, R^{11}, R^{14}, R^{15}, R^{16} and R^{17} are as described, which show an unexpected increase in potency against VEGF and FGF along with an unexpected increase in selectivity with respect to FGF than the 5-heterocyclic thienopyridine compounds of Munchoff. The increased potency and selectivity of the substituted 3-carboxamido-6-heterocyclic compounds is demonstrated by comparing both the enzyme and functional HUVEC cell based assay data shown in Table I to the data provided in Table II for the 5-heterocyclic thienopyridine compounds.

TABLE I
N-Substituted 3-Carboxamido-6-Heterocyclic Thienopyridine Compounds

	FLVK (% inh @ 50 nM)	FLVK Ki (nM)	FGF-P (% inh @ 50 nM)	FGF-P Ki (nM) (% inh @ 1 μM)	HUVEC + VEGF IC_{50} (nM) Avg	bFGF HUVEC IC_{50} (nM) Avg	Ratio HUVEC IC_{50} FGF/ VEGF
	92%	1.02		82%	0.74	210	284
	94%	0.403	15%		1.27	421	331
	88%	2.58	41%		0.404	188	465
	95%	0.438	35%		0.35	108	309
	75%	4.14		51%	1.6	391	244

	90%	0.276	19%		0.24	294	1225
	78%	2.373	0%		2.2	4300	1955
	77%	2.77	0%		2.3	847	368
	100%	0.314			0.26	20	77
	97%	0.322			0.082	27	329
	81%	1.46			9.4	287	30.5
	13%	48.3			NT	NT	
	46%	8.14			10	1,000	100
	77%	2.77			1.2	847	706
	78%	2.373			0.64	1,000	1,563
	75%	2.63			2.7	10,000	3,704

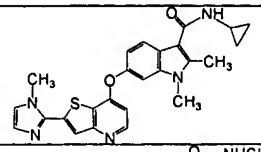
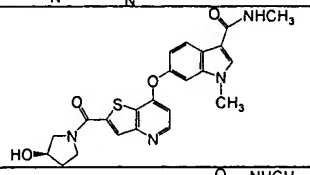
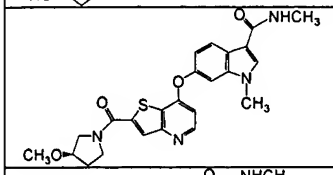
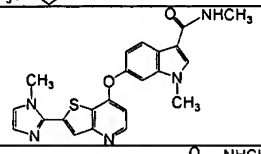
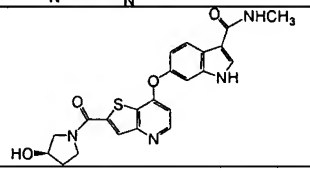
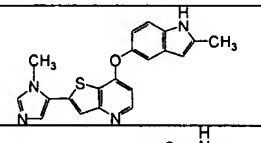
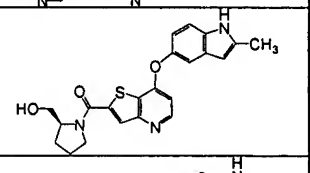
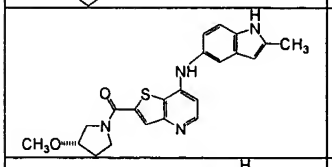
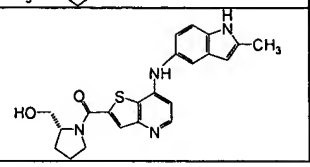
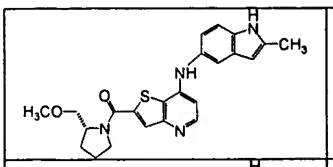
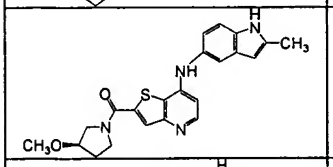
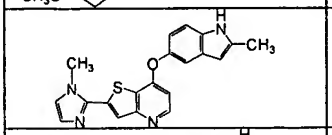
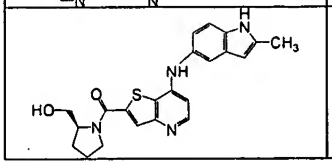
	99%	0.082			0.19	1902	10,011
	43%	13.11			NT	NT	
	38%	25.8			NT	NT	
	19%	78			NT	NT	
	69%	4.2			3.2	10,000	3,125

TABLE II
5-Heterocyclic Thienopyridine Compounds

	FLVK (% inh @ 50 nM)	FLVK Ki (nM)	FGF-P (% inh @ 50 nM)	FGF-P Ki (nM) (% inh @ 1 μM)	HUVEC + VEGF IC_{50} (nM) Avg	bFGF HUVEC IC_{50} (nM) Avg	Ratio HUVEC IC_{50} FGF/ VEGF
	84%	0.8		93%	2	103	52
	71%	0.76		16.2 nM 86%	16	68	4
	46%			91%	11	74	7
	47%			89%	23	29	1

	51%	3.7		87%	15.1	27	2
	67%	1.84		7.5 nM 94%	8.3	165	20
	84%			8.6 nM 93%	0.8	101	126
	41%			45 nM 81%	9.4	150	16

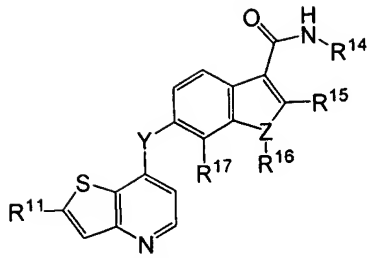
Munchoff does not teach or suggest any N-substituted 3-carboxamido-6-heterocyclic thienopyridine compounds having increased potency against VEGF and FGF and increased selectivity with respect to FGF as required by the claimed compounds. Nor does this reference teach or suggest modifying the 5-heterocyclic thienopyridine compounds taught therein to arrive at the claimed compounds having increased potency and selectivity as described above. Absent a teaching or suggestion in the cited reference, one of skill in the art would not have been motivated to make the claimed class of compounds. Thus, the claimed class of 3-carboxamido-6-heterocyclic thienopyridine compounds is not obvious over the teachings of Munchoff. Applicant respectfully requests reconsideration and removal of this rejection.

Rejection Of Claims Under 35 U.S.C. § 103(a) Over Marx et al. (WO 03/000194)

The Office Action has confirmed the rejection of claims 52-75 and 70-103 under 35 U.S.C. § 103(a) as allegedly being obvious over Marx et al. (WO 03/000194). Applicant respectfully disagrees.

As amended herein, claims 80-101 are canceled, which renders the rejection of these claims moot.

The invention as defined by the claims distinguishes over Marx by claiming N-substituted 3-carboxamido-6-heterocyclic thienopyridine compounds of formula:



wherein Y, Z, R^{11}, R^{14}, R^{15}, R^{16} and R^{17} are as described, which show an unexpected increase in potency against VEGF and FGF along with an unexpected increase in selectivity with respect to FGF than the 5-heterocyclic thienopyridine compounds of Marx. As described above, the increased potency and selectivity of the substituted 3-carboxamido-6-heterocyclic compounds is demonstrated by comparing both the enzyme and functional HUVEC cell based assay data shown in Table I to the data provided in Table II for the 5-heterocyclic thienopyridine compounds.

Marx does not teach or suggest any N-substituted 3-carboxamido-6-heterocyclic thienopyridine compounds having increased potency against VEGF and FGF and increased selectivity with respect to FGF as required by the claimed compounds. Nor does this reference teach or suggest modifying the 5-heterocyclic thienopyridine compounds taught therein to arrive at the claimed compounds having increased potency and selectivity as described above. Absent a teaching or suggestion in the cited reference, one of skill in the art would not have been motivated to make the claimed class of compounds. Thus, the claimed class of 3-carboxamido-6-heterocyclic thienopyridine compounds is not obvious over the teachings of Marx. Applicant respectfully requests reconsideration and removal of this rejection.

Conclusion

Applicants believe all claims are now in condition for allowance. Should there be any issues that have not been addressed to the Examiner's satisfaction, Applicants invite the Examiner to contact the undersigned attorney.

If any fees other than those submitted herewith are due in connection with this response, including the fee for any required extension of time (for which Applicants hereby petition), please charge such fees to Deposit Account No. 500329.

Respectfully submitted,

Date: March 31, 2005

Edward Robinson

Edward D. Robinson
Attorney For Applicant
Registration No. 43,049

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